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THE EFFECT OF HEMIC HYPOXIA THAT OCCURRED IN RATS WITH NITRITE-INDUCED DEMENTIA ON THE DYNAMICS OF BIOCHEMICAL INDICATORS OF ENERGY METABOLISM IN BRAINS

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Abstract. *Have been considered the role of hemic hypoxia, which arose against the background of nitrite-induced dementia of the Alzheimer type in rats on the dynamics in biochemical indicators of energy metabolism, the degree of hypoxia, the content of acetylcholine in the brain tissue homogenate in comparison to the control, where it was found: a decrease in the synthesis and transport of acetylcholine, the intensity of energy exchange, an integral indicator of the decrease in the level of which is the ATP content. The level of cholinodeficiency, hypoxia, and tissue energy supply (ATP) was almost the same between the Nitr-14 and Nitr-28 groups, but the level of cardiolipin in brain homogenates decreased proportionally with increasing duration of sodium nitrite administration.*

Keywords: *nitrite-induced dementia Alzheimer type, brain tissue homogenate, energy metabolism, cholinodeficiency*

Alzheimer's disease is a multifactorial progressive neurodegenerative disease characterized by a violation of protein conformation with subsequent protein aggregation and loss of brain neurons [1,2]. An important role in its progression is played by cerebrovascular and cardiovascular diseases, which cause brain hypoxia [3]. It is known that nerve cells of the brain are very sensitive to hypoxia and energy deficit [4]. In mitochondria, as the main "synthesizers" of ATP, under the influence of hypoxia during the transfer of electrons from the respiratory chain, reactive oxygen species (ROS) are formed due to an excess of which damage to cells and tissues is possible [5,6]. Thus, the issue of the dynamics of changes in biochemical indicators of energy metabolism, and the degree of hypoxia that occurs against the background of nitrite-induced dementia is an actual link of pathogenesis and requires further clarification.

The aim of the study was to determine the effect of hemic hypoxia that occurred in rats with nitrite-induced dementia of the Alzheimer type on the dynamics of biochemical indicators of energy metabolism, the degree of hypoxia, and the content of acetylcholine in brain homogenates.

The study involved 24 male rats from the WAG population, weighing between 180-230g. They were divided into 3 groups, each comprising of 8 rats. The experiment utilized a non-transgenic nitrite-induced model to simulate dementia of the Alzheimer type. The control group (group C) received intraperitoneal injections of 0.5 ml of 0.9% aqueous sodium chloride solution for 14 and 28 days. Nitrite-induced dementia was modeled by administering an aqueous solution of sodium nitrite (Nitr) at a dose of 50 mg/kg per rat daily. Mitochondria were isolated from the brain using the method of differential centrifugation. Separation of lipids into

fractions was carried out by the method of thin-layer chromatography on silica gel plates Silufol (Czech Republic)[7]. To identify the lipids, we exposed them to iodine vapors and compared them to a standard. To determine the cardiolipin content (nmol/mg protein), we used Bartlett G.'s method. We measured the acetylcholine (AC) content (μg/g) and ATP (μmol/g) content in brain homogenates using spectrophotometric methods. We evaluated the normality of the sample distribution using the Shapiro-Wilkie test and used non-parametric tests to compare independent groups of variables based on the results.

The results of the study and their discussion In animals with nitrite-induced dementia, there were noticeable changes in the level of ATP in the rat brain tissue compared to the control group. The level of ATP significantly decreased after 14-day (1.2-fold) and 28-day (1.4-fold) administration of nitrite sodium. Additionally, the concentration of cardiolipin, a crucial lipid in mitochondrial membranes that coordinates the work of oxidative complexes in the respiratory chain, decreased in all studied groups. The most significant decrease was observed in the rats of the Nitr-28 group, with a decrease of 2.3 times (Table 1).

Table 1. Biochemical indicators of energy metabolism, degree of hypoxia, acetylcholine content in rats with nitrite-induced dementia of the Alzheimer type

Indicators	Control group (C)	Group Nitr-14	Group Nitr-28	Гру Nit
AC, μg/g	2,54±0,17 (2) *	2,17±0,07	2,3±0,03 (2) *	2,17
ATP	2,83±0,01 (1) *	2,3±0,01 (C) *	2,03±0,02 (C) *	2,3±0,0
Cardiolipin nmol/mg protein	51,94±0,06 (1) *	26,66±0,1 (C) *	21,84±0,09 (C) *	26,66±0

The data is displayed as the mean values and standard error of the mean.
**p<0.05 - indicates that there is a significant difference between the data of the groups (in parentheses), statistical significance (Kruskal-Wallis analysis of variance and Dunn's multiple comparisons test).*

The introduction of sodium nitrite resulted in a decrease in the level of acetylcholine in the brains of rats in the Nitr-14 and Nitr-28 groups, as compared to the control group (Table 1). These changes in biochemical parameters were significant after 14 and 28 days of sodium nitrite administration. It is worth noting that the levels of cholinodeficiency, hypoxia, and ATP in the Nitr-14 and Nitr-28 groups were similar. However, there was a decrease in the level of cardiolipin in brain homogenates as the duration of sodium nitrite increased.

Conclusions. Based on the experimental data gathered, it has been found that the addition of sodium nitrite plays a crucial role in altering the biochemical indicators of energy metabolism and causing brain hypoxia in rats and is considered to be a relevant link that contributes to the development of Alzheimer's disease.

Under conditions of gaemic hypoxia caused by the introduction of sodium nitrite in the cells and tissues of animals, a low-energy shift occurs in the adenyl system, that is, the synthesis and transport of acetylcholine and the intensity of energy metabolism decrease, the integral indicator of which level is the reduced ATP content.

The level of choline deficiency, hypoxia, and tissue energy supply (ATP) almost does not difference between Nitr-14 and Nitr-28 groups, however, the level of cardiolipin in brain homogenates decreases proportionally with increasing duration of sodium nitrite administration.

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